

## How much can an intermediate state influence competing reactive pathways?

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A molecule undergoing reaction may form a short-lived intermediate. Under certain conditions, the rate at which the reaction proceeds toward the product state via the intermediate may exceed that of a simple, direct path. The competition of two alternative reactive pathways is analyzed here in terms of a stochastic model. The approach allows one to diagnose this competition as a function of the energy of the intermediate relative to the barrier heights of the potential surface and values of the reactive vibrational modes. The result has applications to a variety of problems in chemical physics, ranging from the “lock-and-key” mechanism for the enzymatic activity to control of temporal evolution of complex systems by optimal laser fields. © 2004 American Institute of Physics.

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Under some circumstances, a reaction can proceed with similar rates along distinct pathways with different activation energies. For example, in the model system  $\eta^5\text{-C}_5\text{H}_5\text{Mn}(\text{CO})_3$  photoexcitation and ionization laser pulses lead to equal formation of both the parent molecule ion  $\eta^5\text{-C}_5\text{H}_5\text{Mn}(\text{CO})_3^+$  and the first “daughter ion”  $\eta^5\text{-C}_5\text{H}_5\text{Mn}(\text{CO})_2^+$ .<sup>1</sup> In this experiment, the initial excitation of the system to a neutral excited state ( $b^1A''$ ) prepares the system equally to overcome either the potential barrier toward the parent ion state ( $b^2A'$ )<sup>+</sup> or toward the “daughter ion” ( $a^2A''$ )<sup>+</sup> via an intermediate dissociation channel ( $a^1A''$ ). By applying optimal laser field techniques,<sup>2–5</sup> one can maximize the yield of the organometallic ion while hindering the competing fragmentation.<sup>1</sup> The underlying physics principle of the approach to controlling product selectivity in a reaction can be found mainly in the work of Rice<sup>6</sup> and Brumer and Shapiro.<sup>7</sup> Likewise, there may be two pathways from an initial state to a single final state. Yet there are some intriguing aspects pertaining to the competition between reactive pathways that can be revealed in terms of a stochastic model, and more specifically in terms of the relation between topography of the potential surface (PS) and kinetics. Recently, we developed a way to express such a relation in a practical mathematical form.<sup>8–10</sup> Elements of this approach can be applied to studying reaction dynamics on competing pathways. This is the focus of the present report.

The basic question to be addressed is as follows. Suppose that the system's reaction can take place on two competing pathways to yield the final products  $l$  and  $r$ . (Note that  $l$  and  $r$  may be the same or different.) The reaction path  $l$  is smooth and requires the system to overcome the potential barrier  $E_l$  to complete the reaction. Along the second reaction path  $r$  the effective potential barrier  $E_r$  is higher ( $E_r = E_l + \Delta$ ), but the system has the privilege to overcome this barrier in two easier jumps; first it jumps into the intermediate minimum  $E_i$  separated from the initial state by a local

potential barrier  $E_b$  (see Fig. 1) and, only then, up over the barrier  $E_r$ , toward the final state. We assume that the energies of the three barriers relative to the initial state ( $E_0$ ) plus the vibration frequencies of the reactive modes are known.

What are the depths of the intermediate local minimum  $E_i$  and the barrier heights for which the two escape rate coefficients  $k_r$  and  $k_l$  are equal? We show that there is a range of values for  $\Delta$  and for the intermediate's energy  $E_i$  within which the two reactive pathways are competitive ( $k_r \cong k_l$ ). Outside this range, the system undergoes a clear separation of the two dynamics, with one or the other pathway completely dominant; ( $k_r \neq k_l$ ). The issue can also be expressed in terms of Fourier components of the reaction coordinate. For a given (imposed) topography of the characteristic PS, equal escape rate coefficients ( $k_l = k_r$ ) can be achieved by tuning the vibration frequencies of the reactive modes. The present investigation improves our understanding about competing reactive pathways and points to interesting new features of the mechanism of controlling chemical reactions. The results may prove valuable in selecting further new systems suitable for laser-induced dynamics. In addition, our results bring the mathematical formulation of enzymatic activity to a perspective from which we can infer not only the role of the barrier heights along a reaction path, but also the influence of the vibrational frequencies and intermediate, short-lived but equilibrated states on the relative importance of specific pathways. Before entering further details the following comments have to be in order. The present approach is a particular case of the more general problem of multiple competing paths.<sup>11</sup> This applies to one-dimensional reaction trajectories and remains valid, however curvilinear they may be, so long as the reaction coordinate separates from the other degrees of freedom.<sup>12</sup>

Let us assume that the reaction occurs along the pathway  $l$  when the molecule acquires a certain critical energy  $E_l$ . As the system approaches the transition state  $E_l$ , the reaction mode  $l$  starts decoupling from the others.<sup>12,13</sup> Under such a circumstance, one can describe the changes in energy of the

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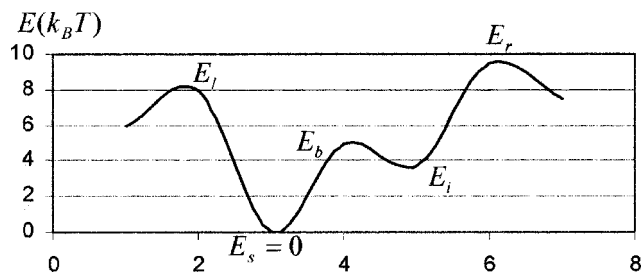


FIG. 1. The archetype of potential surface (PS) yielding competing reactive pathways.

reaction mode  $l$  in terms of a stochastic, one-degree-of-freedom process.<sup>14</sup> Accordingly, the time to reach  $E_l$  from the starting point  $E_s$  (which, usually, coincides with the bottom of the potential well,  $E_s=0$ ) is

$$\tau_l(E_s, E_l) = \int_{E_s}^{E_l} dE \frac{\exp(\beta E)}{\mu_l(E)} \int_0^E dE' \frac{\exp(-\beta E')}{\omega_l(E')} \quad (1)$$

Similar equations describe  $\tau_b(E_s, E_b)$  and  $\tau_r(E_i, E_r)$  for the individual steps along the right-hand pathway of Fig. 1. Here,  $\tau_l$  depends on both the vibrational frequency function  $\omega_l(E)$  and the corresponding energy diffusion coefficient  $\mu_l(E)$ ;  $\beta$  has its usual meaning  $\beta=1/k_B T$ . The key frequency is usually derived from the specific form of the potential ( $V_{\text{eff}}$ ) along the reaction pathway. Here,  $\omega_l(E)$  is the absolute value of the (imaginary) vibrational frequency of the reactive mode  $l$  in the barrier region and is approximated by a harmonic oscillator of frequency  $\omega_l$ . The corresponding energy diffusion coefficient is<sup>8</sup>

$$\mu_l(E) = \frac{E\gamma}{\beta\omega_l} \exp(-\rho_l^2), \quad (2)$$

where  $\gamma$  represents the damping rate of the environment and  $\rho_l$  is the reduced frequency parameter,  $\rho_l = \omega_l t_c$ , with  $t_c$  standing for the correlation time.  $\gamma$  is associated with the coupling to the thermal bath and is related to the random force  $R(t)$  acting on the system through the fluctuation-dissipation theorem  $\langle R(0)R(t) \rangle = 2\gamma M (\delta(t)/\beta)$ .  $M$  represents the mass of the particle and  $\delta(t)$  is the  $\delta$  function that returns 0 for all  $t$  other than 0. For a particle embedded in a solvent  $\gamma$  depends on the viscosity of the solvent and on the shape of the particle.<sup>9</sup>  $t_c$  is a measure of the extent or rate of equipartition of the reaction mode  $\omega_l$  with the thermal bath consisting of the other, nonreactive modes. The meaning of Eq. (1) is the following: If initially the random variable of interest lies in the region of the configuration space  $\Omega_0$  with  $E < E_l$ ,  $\tau_l(0, E_l)$  is the mean time for the first passage to the region of the configuration space  $\Omega_l$  with  $E \geq E_l$ .

Moving along the competing pathway  $r$  the system first reaches the intermediate state  $E_i$  in the region  $\Omega_i$  of the configuration space. The mean first passage time here is  $\tau_b(0, E_b)$  and corresponds to the energy accumulation  $E_b$  in the reactive mode  $\omega_b$ . A subsequent motion upward on the energy scale in a time  $\tau_r(E_i, E_r)$  leads the system along the reactive mode  $r$  in the final state  $r$ . The following observation can be made. Due to the exponential character of Eq. (1),  $\tau_l(0, E_l) \geq \tau_b(0, E_b) + \tau_r(E_i, E_r)$  in the appropriate range

of values for  $E_i$ . Consequently, the system can relax in the intermediate state  $E_i$ , accumulate energy for the final step over the barrier placed at the energy  $E_r$ , and still reach the final state  $r$  in a time comparable with  $\tau_l$ .

The mean first passage time Eq. (1) is based on the reduced Fokker-Planck equation<sup>14</sup>

$$\frac{\partial P}{\partial t} = \frac{\partial}{\partial E} \left[ \mu(E) \left( \frac{\partial}{\partial E} + \beta \right) \right] \omega(E) P, \quad (3)$$

which is a formulation of a stochastic, one-degree-of-freedom process for the energy  $E$  in the unstable mode  $\omega(E)$ . A steady-state ( $\partial P/\partial t = 0$ ) solution of Eq. (3) for the reactive pathway  $l$  is given by

$$P_l(E) = \begin{cases} A_0 \exp(-\beta E), & 0 \leq E \leq E_0 \\ F_l(E) \exp(-\beta E), & E_0 < E \leq E_l \end{cases} \quad (4)$$

$A_0$  is the probability density that the system be at the bottom of the well and  $F_l$  is a "correction function" given by

$$F_l = A_0 - A \int_{E_0}^E dE' \frac{\exp(\beta E')}{\mu_l(E')}.$$

$F_l$  converts the typical Kramers description of the quasi-steady-state situation, in which the escape is slow relative to the other time scales in the system and requires a deep enough potential well, to a real steady state. A steady-state situation is mathematically realized by providing a source at or near the bottom of the well that keeps the distribution at  $0 \leq E \leq E_0$  of a Boltzmann form. The final rate does not depend on the choice of  $A_0$  and  $E_0$ . The parameter  $A$  is to be determined from the normalization condition. The steady-state current associated with Eq. (4) is obtained by using

$$j_l = -\mu_l(E) \left( \frac{dP_l}{dE} + \beta P_l \right), \quad (5)$$

which yields  $j_l = A/\beta$ . The escape rate is taken to be this flux divided by the population undergoing the reaction along the pathway  $l$ ,  $k_l = A/\beta N_l$ .<sup>15,16</sup> The number of particles taking this path,  $N_l$ , is given by

$$N_l = \int_0^{E_l} dE P_l(E). \quad (6)$$

We now turn to the task of evaluating the escape rate of the system on the competing pathway  $r$ . First, the system is activated over the potential barrier  $E_b$  that leads the system toward the intermediate state. The probability density of the process reads

$$P_b(E) = \begin{cases} A_0 \exp(-\beta E), & 0 \leq E \leq E_0 \\ \left( A_0 - B \int_{E_0}^E dE \frac{\exp(\beta E)}{\mu_b(E)} \right) \exp(-\beta E), & E_0 < E \leq E_b \end{cases} \quad (7)$$

From the intermediate state  $E_i$  the system can either return to the initial state by activation of the mode  $\omega_i$  that passes the system back over the barrier  $E_b$ , or reach the energy  $E_r$  in the reactive mode  $\omega_r$  and complete the reaction. The probability density corresponding to the former is

$$P_i(E) = \left( C_0 - C \int_{E_i}^E \frac{\exp(\beta E)}{\mu_i(E)} \right) \exp(-\beta E), \quad E_i \leq E \leq E_b, \quad (8)$$

while the latter is described by

$$P_r(E) = \left( C_0 - D \int_{E_i}^E \frac{\exp(\beta E)}{\mu_r(E)} \right) \exp(-\beta E), \quad E_i \leq E \leq E_r. \quad (9)$$

In the above,  $C_0$  measures the density of population at the bottom of the intermediate well  $i$ ,  $C_0 = A_0 \exp(-\beta E_i)$ . In the steady state, the current must be the same everywhere and therefore  $A = B = C = D$ . The normalized current  $k_r = A/\beta N_r$  gives the escape rate along the reactive pathway  $r$ .<sup>16</sup> The population along the reactive path  $r$ ,  $N_r$ , is

$$N_r = \int_0^{E_b} dE P_b(E) + \int_{E_i}^{E_b} dE P_i(E) + \int_{E_i}^{E_r} dE P_r(E). \quad (10)$$

The normalization condition  $N_r + N_l = N$ , where  $N$  is the entire population of the well, allows us to determine  $A$  in the above,

$$\frac{\beta A}{A_0} = \frac{1}{\Phi_1(E_i)} \left( 2 - e^{-\beta E_l} - e^{-\beta E_b} + 2e^{-2\beta E_i} - e^{-\beta(E_b+E_i)} - e^{-\beta(E_r+E_i)} - \frac{N\beta}{A_0} \right), \quad (11)$$

$$\begin{aligned} \Phi_1(E_i) &= \int_{E_0}^{E_b} dE e^{-\beta E} \int_0^E dE \frac{e^{\beta E}}{\mu_b(E)} \\ &+ \int_{E_i}^{E_b} dE e^{-\beta E} \int_0^E dE \frac{e^{\beta E}}{\mu_i(E)} \\ &+ \int_{E_i}^{E_r} dE e^{-\beta E} \int_0^E dE \frac{e^{\beta E}}{\mu_r(E)} \\ &+ \int_{E_0}^{E_i} dE e^{-\beta E} \int_0^E dE \frac{e^{\beta E}}{\mu_i(E)}. \end{aligned}$$

Under these circumstances, a competition ( $k_r = k_l$ ) between the two reactive pathways occurs when  $N_r = N_l$ ; The conditions for this balance depend on the position on the energy scale of the intermediate level  $i$ . The energy level  $E_i$  is the solution of this equation:

$$\frac{\beta A}{A_0} = \frac{1}{\Phi_2(E_i)} (e^{-\beta E_l} - e^{-\beta E_b} + 2e^{-2\beta E_i} - e^{-\beta(E_b+E_i)} - e^{-\beta(E_r+E_i)}), \quad (12)$$

$$\begin{aligned} \Phi_2(E_i) &= \int_{E_0}^{E_b} dE e^{-\beta E} \int_0^E dE \frac{e^{\beta E}}{\mu_b(E)} \\ &+ \int_{E_i}^{E_b} dE e^{-\beta E} \int_0^E dE \frac{e^{\beta E}}{\mu_i(E)} \\ &+ \int_{E_i}^{E_r} dE e^{-\beta E} \int_0^E dE \frac{e^{\beta E}}{\mu_r(E)} \\ &- \int_{E_0}^{E_i} dE e^{-\beta E} \int_0^E dE \frac{e^{\beta E}}{\mu_i(E)}. \end{aligned}$$

Equivalently, by replacing for  $\beta A/A_0$  from Eq. (12) we get

$$\frac{e^{-\beta E_l} - e^{-\beta E_b} + 2e^{-2\beta E_i} - e^{-\beta(E_b+E_i)} - e^{-\beta(E_r+E_i)}}{2 - e^{-\beta E_l} - e^{-\beta E_b} + 2e^{-2\beta E_i} - e^{-\beta(E_b+E_i)} - e^{-\beta(E_r+E_i)} - \frac{N\beta}{A_0}} = \frac{\Phi_2(E_i)}{\Phi_1(E_i)}. \quad (13)$$

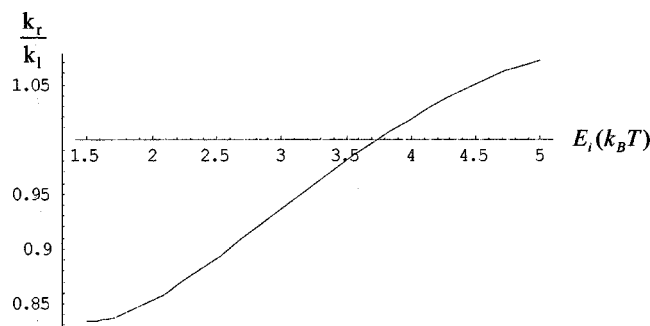


FIG. 2. The energy of the intermediate state  $E_i$  that equilibrates the currents along the two reactive pathways ( $k_r/k_l$ ).

We have checked this point numerically for the PS of Fig. 1 for  $E_l = 8.5 k_B T$ ,  $E_b = 5 k_B T$ ,  $E_r = 9.5 k_B T$ ,  $\omega_l = \omega_b = \omega_i = 10\gamma$ ,  $\rho_l = \rho_b = \rho_i = 1$ ,  $\omega_r = 8\gamma$ , and  $\rho_r = 0.8$ . Usually, “internal frictions” set  $\gamma$  at about  $\sim 10^{12} \text{ s}^{-1}$ , hence  $\omega_{l,b,i,r} \sim 10^{13} \text{ s}^{-1}$ . However, for a particle embedded in a solvent,  $\gamma$  spans a wide range of values lower with orders of magnitude below  $10^{12} \text{ s}^{-1}$ . The energy of the intermediate state that equates the currents along the two reactive pathways is  $E_i = 3.75 k_B T$  (see Fig. 2). A simple calculation with Eq. (1) gives, under such conditions,  $\tau_l(0, E_i) = \tau_b(0, E_b) + \tau_i(E_i, E_b) + \tau_r(E_i, E_r)$ . Figure 2 shows that an increase of  $E_i$  over  $3.75 k_B T$  brings the system to follow the pathway to the product  $r$  with a higher rate ( $k_r > k_l$ ). Otherwise, if  $E_i$  is less than  $3.75 k_B T$  the reactive pathway  $r$  is slower than  $l$ . We have found that, for our chosen values of  $E_l$ ,  $E_b$  and vibration frequencies, the upper limit of  $\Delta$  for which the two paths have competitive rates is about  $1.7 k_B T$ . Any increase over this limit makes the reactive pathway  $r$  slower than  $l$  regardless of the position of the intermediate state.

We can ask the parallel question of how the position on the energy scale of the intermediate barrier  $E_b$  affects the selectivity of the reactive pathway. The behavior of  $k_r/k_l$  as a function of  $E_b$  can be seen in Fig. 3. The range of variation here for  $E_b$  is between  $4 k_B T$  and  $8 k_B T$ . All other parameters are kept at the values given above and  $E_i$  is placed at  $3.75 k_B T$ . Under such conditions, we note that potential barriers higher than about  $5 k_B T$  turn the system to go faster along the reactive pathway  $l$ , a result that could already be inferred from Fig. 2.

Similar results can be achieved by tuning the vibration frequencies of the reactive modes. In Fig. 4 we displayed

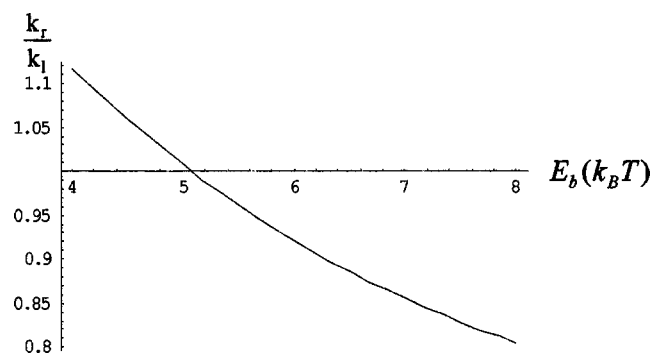


FIG. 3. The behavior of  $k_r/k_l$  as a function of the barrier height  $E_b$ .

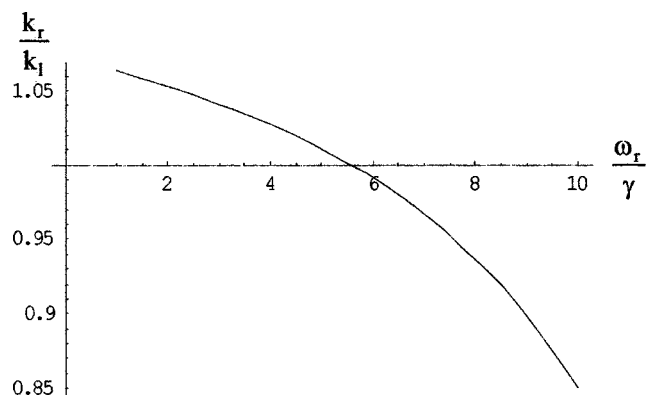


FIG. 4.  $k_r/k_l$  as a function of the vibration frequency in the reactive mode  $\omega_r$ .

$k_r/k_l$  as a function of the vibration frequency in the reactive mode  $\omega_r$ . The competition between the two reactive pathways is influenced by the dynamics near the potential barriers on the PS (see Fig. 1 for the energy values of minima and saddles). For a constant value of the correlation time  $\tau_c = 0.1\gamma^{-1}$  the reaction product  $r$  can be obtained at fast or slow rates depending on the the vibration frequency  $\omega_r$  relative to the damping rate  $\gamma$ . This shows that the vibrational energy transfer plays a role in stabilizing the product molecule. (It should be kept in mind that the actual time of relaxation is determined not by  $\gamma$  but by the spectral density of the time-dependent friction function.<sup>14</sup>) The last observation points to the systems with sufficiently large densities of states along the pathways leading to the target. The reactive modes with low vibration frequencies in the barrier region are important for stabilizing the reaction. This is an important result for its implication about controlling temporal evolution of complex systems by optimal laser fields,<sup>2-6</sup> especially insofar as it reveals the relevant range of the reference laser pulse frequency. It should be possible to select the desired product while suppressing the competing channels by means of well-designed subpulses with frequencies around the reference value.

Another area where the present theory will be useful is in achieving a better understanding of the quantitative aspects of enzymatic activity: The rate at which a reaction proceeds to form the product depends on the position on the energy scale of the short-lived intermediate (the enzyme-substrate complex). Enzymes are thought to operate on a “lock and key” mechanism.<sup>17</sup> In the same way that a key fits a lock very precisely, so the substrate fits accurately into the active site of the enzyme molecule. The two molecules form a temporary structure called the enzyme-substrate complex. The products have a different shape from the substrate and so, once formed, they escape from the active site, leaving it free to become attached to another substrate molecule. Other, more recent, interpretations of the lock and key mechanism suggest that in the presence of the appropriate substrate the active site may change in order to suit the substrate’s shape. The enzyme is flexible and moulds to fit the substrate molecule. Our results brings the mathematical formulation of the enzymatic activity to a modern perspective from which we can infer not only the role of the motion up and down of the

barrier heights involved in reaction, but also the influence of the vibrational frequencies on the efficiency of promoting that reaction along a specific pathway. Therefore, the present approach can be seen as an alternate quantitative expression of E. Fischer's "lock-and-key" mechanism.

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